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UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

GEN-PROBE INCORPORATED,

Plaintiff,

v.

VYSIS, INC.,

Defendant.

No. 99-CV-2668H AJB
JUDGE MARILYN L. HUFF

DECLARATION OF DR. MATTHEW LONGIARU IN SUPPORT OF GEN-PROBE'S MOTION FOR PARTIAL SUMMARY JUDGMENT

Date: May 29, 2001
Time: 10:30 a.m.
Dept: Courtroom 1

I, Mat Longiaru, declare as follows:

1. I am employed by plaintiff Gen-Probe Incorporated as Vice President, Diagnostic Development. I have been employed by Gen-Probe since February 1991.

2. As disclosed in my *Curriculum* Vitae attached hereto as Exhibit 1, I received a B.S.

(Biology) from the City College of New York in 1975, an M.S. (Microbiology) from Long Island University in 1977, and a Ph.D. (Microbiology and Immunology) from Albert Einstein College of Medicine in 1981.

3. As a result of my education and experience, I am familiar with methods of nucleic acid target capture and amplification. I understand methods of non-specific amplification as disclosed in the examples by U.S. Patent No. 5,750,338 ("the '338 patent") and methods of specific amplification, such as Gen-Probe's patented Transcription-Mediated Amplification (TMA) process.

4. I have read the Scientific Background section of the accompanying memorandum in support of summary judgment. The Scientific Background section presents an accurate summary of information about the nucleic acid methods discussed therein.

TMA Uses Sequence-Specific Primers to Achieve Specific Amplification

5. Gen-Probe's HIV-1/HCV Assay ("the Blood Screening Assay") detects small quantities of HIV (human immunodeficiency virus) and HCV (hepatitis C virus) in blood by capturing the viral nucleic acids (i.e., the target nucleic acids) from a sample of blood and amplifying them. The Blood Screening Assay incorporates Gen-Probe's patented TMA technology to *specifically* amplify the captured viral nucleic acids

6. Gen-Probe's Blood Screening Assay achieves specific amplification in part by employing sequence-specific primers, which are designed and made to bind only to specific sequences of interest in the target HIV and HCV nucleic acids. The TMA process will only amplify nucleic acid captured from a sample if the primers find and bind to their respective specific target sequences.

7. One of the two enzymes used in Gen-Probe's Blood Screening Assay is reverse transcriptase ("RT"). Reverse transcriptase is a DNA polymerase that produces a complementary DNA strand copy of a single-stranded RNA or DNA that has a bound primer. In TMA, reverse transcriptase produces complementary DNA from the target nucleic acids (or their complementary strands) only if the sequence-specific primers (described in paragraph 6) first bind to a single strand of RNA or DNA. That is, if the target organism is not present in the sample, the primers

will be unable to bind to the captured sequence and the reverse transcriptase will not initiate synthesis. Therefore the action of the RT enzyme is dependent on the specific primers.

TMA Also Uses Specific Promoters and Enzymes to Achieve Specific Amplification

8. In addition to its target-specific sequence, some of the TMA primers used in the Blood Screening Assay contain a "promoter" sequence that allows a specific enzyme, an RNA "T7 polymerase," to *specifically* bind to and produce RNA copies of the target nucleic acids as part of the TMA amplification process.

9. A functional "T7 promoter" is formed in the course of the TMA process if, and only if, the primer finds and binds to its complementary target sequence in the captured target molecule so that the target sequence is copied by reverse transcriptase. If the T7 promoter *is* formed as a result of primer binding to the target sequence, then the T7 RNA polymerase used in Gen-Probe's Blood Screening Assay will amplify the sequence attached to the T7 promoter sequence. The T7 RNA polymerase does not amplify other sequences present in the sample because they are not attached to a T7 promoter sequence. Thus, in the Blood Screening Assay, the T7 polymerase enzyme *specifically* recognizes the T7 promoter sequence, which has been *specifically* attached to the target sequence by the binding of *specific* primers, and the T7 polymerase *specifically* amplifies only that sequence.

10. In the TMA process, one of the primers *specifically* binds to the newly transcribed RNA and reverse transcriptase makes a new complementary DNA copy of that RNA. The process repeats in a cyclic fashion, resulting in exponential amplification only of the particular target sequence of interest as a consequence of the use of sequence-specific primers, specific promoter sequences, and specific RNA polymerase enzymes. This process safeguards against amplification of non-target sequences and thus protects against false positive results.

11. The TMA method used in the Blood Screening Assay differs substantially from the non-specific amplification methods disclosed in the '338 patent. All of the methods described in the examples of the '338 patent *non-specifically* amplify any nucleic acids captured from the sample, whether those nucleic acids are the intended target or are some other nucleic acid present in the sample after target capture. Unlike the non-specific amplification methods described in the

'338 patent, the TMA process will not amplify non-target sequences that might be retained on the solid support after the target capture step. The sequence-specific primers, specific promoters, and specific RNA polymerase enzymes used in TMA are designed to only amplify their intended target nucleic acids, even if other sequences are present.

I hereby declare under penalty of perjury under the laws of the United States of America that all statements made herein of my own knowledge true and that all statements made on information and belief are believed to be true. This declaration was executed by me on this 24 day of April, 2001 at San Diego, California.

Matthew Longiaru